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TITLE: Pharmacogenomic Strategies to Refine Cisplatin Therapy in Lung Cancer

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14. ABSTRACT

Gene expression signatures can predict in vitro and in vivo response to chemotherapy, including cisplatin, allowing patients to be matched with chemotherapy their tumor has been predicted to be sensitive to, in order to maximize response to the drug and potentially improve survival. A gene expression signature of cisplatin sensitivity is currently being validated in an ongoing prospective phase II trial of stage IIIb/IV NSCLC, expected to complete accrual by mid-2010. Patients predicted to be sensitive to cisplatin will receive cisplatin/gemcitabine, and those predicted to be resistant to cisplatin will receive gemcitabine/pemetrexed. This provides opportunity for refinement of this chemotherapy sensitivity predictor. We will pursue broadening the development of chemosensitivity predictors to a formalin-fixed paraffin-embedded (FFPE) based assay. This will allow FFPE tissues samples, which are more readily available for prospective clinical trials than traditionally required fresh frozen tissue samples, to be used to identify patients more likely to respond to a specific chemotherapeutic agent. Lastly, since the ERCC1 (excision repair cross-complementing) gene family decreases DNA damage by nucleotide excision and repair, potentially affecting platinum-based therapy, we plan to evaluate if ERCC1 status is complementary and can be integrated with a genomic predictor of cisplatin sensitivity in our study patients. This grant was terminated prior to any work being started or completed towards its goals.

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Table of Contents

Introduction

Gene expression signatures can predict in vitro and in vivo response to chemotherapy, including cisplatin, allowing patients to be matched with chemotherapy their tumor has been predicted to be sensitive to, in order to maximize response to the drug and potentially improve survival. A gene expression signature of cisplatin sensitivity is currently being validated in an ongoing prospective phase II trial of stage IIIb/IV NSCLC, expected to complete accrual by mid-2010. Patients predicted to be sensitive to cisplatin will receive cisplatin/gemcitabine, and those predicted to be resistant to cisplatin will receive gemcitabine/pemetrexed. This provides opportunity for refinement of this chemotherapy sensitivity predictor. We will pursue broadening the development of chemosensitivity predictors to a formalin-fixed paraffin-embedded (FFPE) based assay. This will allow FFPE tissues samples, which are more readily available for prospective clinical trials than traditionally required fresh frozen tissue samples, to be used to identify patients more likely to respond to a specific chemotherapeutic agent. Lastly, since the ERCC1 (excision repair cross-complementing) gene family decreases DNA damage by nucleotide excision and repair, potentially affecting platinum-based therapy, we plan to evaluate if ERCC1 status is complementary and can be integrated with a genomic predictor of cisplatin sensitivity in our study patients.

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Body

NA

Key Research Accomplishments

NA

Reportable Outcomes

NA

Conclusion

NA

References

NA

Appendices

NA